

---

**Depletion of Tcf3 and Lef1 maintains mouse embryonic stem cell self-renewal.**

**Journal:** Biol Open

**Publication Year:** 2017

**Authors:** Shoudong Ye, Tao Zhang, Chang Tong, Xingliang Zhou, Kan He, Qian Ban, Dahai Liu, Qi-Long Ying

**PubMed link:** 28288968

**Funding Grants:** Self-renewal of human embryonic stem cells, Mechanisms Underlying the Diverse Functions of STAT3 in Embryonic Stem Cell Fate Regulation

**Public Summary:**

Embryonic stem cells (ESCs) are pluripotent stem cells that can give rise to every cell type in the body. Understanding how ESCs are maintained holds great promise for developing regenerative medicine and cell therapies. In this study, we investigated the function of two genes, Tcf3 and Lef1, in the regulation of mouse ESC fate. We found that Tcf3 and Lef1 play critical roles in inducing ESC differentiation. Genetic deletion of both Tcf3 and Lef1 is sufficient to maintain ESC self-renewal. Our finding further supports the notion that the key to maintaining ESC state is to block differentiation signals.

**Scientific Abstract:**

Mouse and rat embryonic stem cell (ESC) self-renewal can be maintained by dual inhibition of glycogen synthase kinase 3 (GSK3) and mitogen-activated protein kinase kinase (MEK). Inhibition of GSK3 promotes ESC self-renewal by abrogating T-cell factor 3 (TCF3)-mediated repression of the pluripotency network. How inhibition of MEK mediates ESC self-renewal, however, remains largely unknown. Here, we show that inhibition of MEK can significantly suppress lymphoid enhancer factor 1 (LEF1) expression in mouse ESCs. Knockdown or knockout of Lef1 partially mimics the self-renewal-promoting effect of MEK inhibitors. Moreover, depletion of both Tcf3 and Lef1 enables maintenance of undifferentiated mouse ESCs without exogenous factors, cytokines or inhibitors. Transcriptome resequencing analysis reveals that LEF1 is closely associated with endoderm specification in ESCs. Thus, our study adds support to the notion that the key to maintaining the ESC ground state is to shield ESCs from differentiative cues.

---

**Source URL:** <https://www.cirm.ca.gov/about-cirm/publications/depletion-tcf3-and-lef1-maintains-mouse-embryonic-stem-cell-self-renewal>